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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,212	10/01/2003	Frank X. Chen	CD01613K	9696
24265	7590	09/20/2004	EXAMINER	
SCHERING-PLOUGH CORPORATION PATENT DEPARTMENT (K-6-1, 1990) 2000 GALLOPING HILL ROAD KENILWORTH, NJ 07033-0530			HUANG, EVELYN MEI	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 09/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/676,212

Applicant(s)

CHEN ET AL.

Examiner

Evelyn Huang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 August 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 14-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

1. Claims 1-19 are pending.

Election/Restrictions

2. In response to the restriction requirement mailed on 6-9-2004, applicant has elected with traverse the Group I invention, i.e. claims 1-13. Claims 14-19 of Group II-IV are withdrawn from further consideration as being drawn to the non-elected invention.

Applicant maintains that a thorough search of one group would cover the other groups of invention because the product of Group II process is used in the process of Group I, the product of Group I is used in the process of Group III, and the product of Group III is used in the process of Group II. Applicant request rejoining Group III with Group I.

On the contrary, Groups I-IV are different processes for making different products employing different starting materials via different reactions. For example, the product of Group I can be prepared by a materially different process as disclosed by Bernard (6372909, PTO-1449). The product of Group III can be prepared by the process described in 5719148 (PTO-1449). These inventions are distinct and have acquired a separate status in the art. A reference anticipating one group of invention would not render obvious the other groups of inventions. The search is not co-extensive and is therefore burdensome. Since the search required for one group is not required for the other groups, restriction for examination purposes as indicated is proper.

Upon allowance of the Group I claims, claims 17, 18 of Group III can be rejoined if the process of Group I were incorporated into claims 17, 18, or if they were dependent on the Group I process claims.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- a. Claim 1,
 - Definition of R of formula XI, 'heteroarryl' should be 'heteroaryl'.
 - For the 'organic ether or amine additive', does it include petroleum ether, crown ether, cyclic amine etc? it is recommended that the definition on page 9 be recited in the claim.
- b. Claim 7, line 2, it is recommended that 'to' be inserted between 'water' and 'the reaction mixture' to better define the claim.
- c. Claim 8, it is recommended that 'the resulting reaction mixture formed by the adding water' be amended to -- the resulting reaction mixture formed by the process of claim 7 --.

The rejection is applicable to claims dependent on the above claims.

Duplicate Claims

4. Claim 3 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. The 'organic ether or amine additive is an alkyl ether, an alkylamine, an arylamine' in claim 3 is the full definition of 'organic ether or amine additive' of claim 1 as disclosed in the specification. The scope of these two claims are therefore identical. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, is only enabling for the process wherein the leaving group in formula X is sulfonate, the organic ether or amine additive is as defined in claim 4, the non-nucleophilic strong base as defined in claim 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

a. *Nature of the invention.*

The instant invention is drawn to an enantioselective process of preparing a compound of formula VI comprising contacting a compound of formula V with a reaction mixture comprising a chiral amino alcohol, a compound of formula X and an organic ether or amine additive followed by addition of a non-nucleophilic strong base.

b. *State of the prior art and the level of the skill in the art.*

Enantioselective carbon-carbon bond forming reactions have been described, the anion that is generated and alkylated mostly has an adjacent carbonyl type stabilizing group such as ketone (Tomioka et al., Chem. Pharm. Bull. 1989, 37(4):1120-1122). Enantioselective alkylation of tricyclic compound similar to the instant has been described by Kuo (6307048, PTO-1449).

The level of the skilled in the chemical synthetic art is high.

c. *Predictability/unpredictability of the art.*

Unlike the mechanical art, the high degree of unpredictability is well recognized in the chemical synthetic art. A change in the structure of the reactants may drastically affect the rate of the chemical reaction. For example, dramatic leaving group effect has been demonstrated on the enantioselectivity of the alkylation process (Tomioka, page 1121, Table 1).

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d. *Amount of guidance/working examples.*

The exemplified process are limited to the use of quinine, the compound of formula X having sulfonate as leaving group, the non-nucleophilic strong base being LDA, Li N-butyl, N-phenylamide, or Li N-ethyl-phenylamide, and the organic amine or ether additive being t-BuOme, TMEDA, isopropylamine, isopropylaniline, ethylaniline, N-phenyl, N-benzylamine/TMEDA or N-phenyl, N-naphthylamine.

e. *The breadth of the claims.*

Applicant's assertion that all the different chiral amino alcohols of formula XI or XII, any organic ether or amine additive, any non-nucleophilic strong base, formula X with any leaving group would lead to the instant enantioselective process, does not commensurate with the scope of the objective enablement, especially in view of the high degree of unpredictability in the art and the limited working examples (paragraphs c, d above).

f. *Quantitation of undue experimentation.*

Since insufficient teaching and guidance have been provided in the disclosure, one of ordinary skill in the art, even with high degree of skill, would not be able to make and use all the compounds as claimed without undue experimentation.

Conclusion

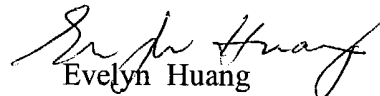
6. Kuo (6307048, PTO-1449) discloses an enantioselective alkylation process of making a benzocycloheptapyridine-piperidinyl compound similar to the instant. The instant process, having enhanced enantioselectivity (page 33 of the specification), employs an additional organic ether or amine additive in the reaction. Motivation to modify Kuo's process to arrive at the instant is lacking.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Evelyn Huang', is positioned above the printed name.

Evelyn Huang

Primary Examiner

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